- (4) *Moisture.* Proceed as directed in §436.201 of this chapter.
- (5) pH. Proceed as directed in §436.202 of this chapter, using a concentration of 60 milligrams of rifampin per milliliter
- (6) *Identity*. Proceed as directed in §436.365 of this chapter.

[54 FR 38375, Sept. 18, 1989]

§ 455.280a Sterile spectinomycin hydrochloride.

The requirements for certification and the tests and methods of assay for sterile spectinomycin hydrochloride packaged for dispensing are described in §455.80a.

§ 455.285 Vancomycin hydrochloride injectable dosage forms.

§455.285a Sterile vancomycin hydrochloride.

The requirements for certification and the tests and methods of assay for sterile vancomycin hydrochloride packaged for dispensing are described in §455.85a.

§ 455.285b Vancomycin hydrochloride for injection.

(a) Requirements for certification—(1) Standards of identity, strength, quality, and purity. Vancomycin hydrochloride for injection is a dry mixture of vancomycin hydrochloride and a suitable stabilizing agent. It contains not 925 than micrograms vancomycin per milligram, calculated on an anhydrous basis. Its vancomycin content is satisfactory if it is not less than 90 percent and not more than 115 percent of the number of milligrams of vancomycin that it is represented to contain. It contains not less than 88 percent vancomycin factor B. It contains not more than 4 percent of any individual vancomycin related factor. It is sterile. It is nonpyrogenic. Its moisture content is not more than 5 percent. The pH of an aqueous solution containing 50 milligrams per milliliter is not less than 2.5 and not more than 4.5. Its heavy metals content is not more than 30 parts per million. It gives positive identity test. The vancomycin hydrochloride used conforms to the standards prescribed by § 455.85(a)(1).

- (2) Labeling. It shall be labeled in accordance with the requirements of § 432.5 of this chapter.
- (3) Request for certification; samples. In addition to the requirements of §431.1 of this chapter, each such request shall contain:
- (i) Results of tests and assays on:
- (A) The vancomycin hydrochloride used in making the batch for potency, moisture, pH, factor A content, and identity.
- (B) The batch for vancomycin potency, vancomycin content, chromatographic purity, sterility, pyrogens, moisture, pH, heavy metals, and identity.
- (ii) Samples, if required by the Director, Center for Drug Evaluation and Research:
- (A) The vancomycin used in making the batch: 10 packages, each containing approximately 500 milligrams.
 - (B) The batch:
- (1) For all tests except sterility: A minimum of 10 immediate containers.
- (2) For sterility testing: 20 immediate containers, collected at regular intervals throughout each filling operation.
- (b) Test and methods of assay—(1) Vancomycin potency and content. Determine both micrograms of vancomycin per milligram of sample and milligrams of vancomycin per container. Proceed as directed in §435.105 of this chapter, preparing the sample solution as follows:
- (i) Preparation of sample solution. Use separate containers for preparation of each sample solution as described in paragraphs (b)(1)(i) (A) and (B) of this section.
- (A) Micrograms of vancomycin per milligram. Dissolve an accurately weighed sample of approximately 30 milligrams in sufficient distilled water to obtain a stock solution of 1 milligram per milliliter. Further dilute an aliquot of the stock solution with 0.1M potassium phosphate buffer, pH 4.5 (solution 4) to the reference concentration of 10.0 micrograms of vancomycin per milliliter (estimated).
- (B) Milligrams of vancomycin per container. Reconstitute as directed in the labeling. Using a suitable hypodermic needle and syringe, remove all of the withdrawable contents if it is represented as a single-dose container; or,

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if the labeling specifies the amount of vancomycin content in a given volume of the resultant preparation, remove an accurately measured representative portion from each container. Dilute with 0.1*M* potassium phosphate buffer, pH 4.5 (solution 4) to the reference concentration of 10.0 micrograms of vancomycin per milliliter (estimated).

(2) Chromatographic purity. Proceed as directed in § 436.366 of this chapter. The relative amount of vancomycin B is not less than 88 percent and the relative amount of any related substance is not more than 4 percent.

(3) Sterility. Proceed as directed in §436.20 of this chapter, using the method described in paragraph (e)(1) of that section, except use sterile distilled water in lieu of diluting fluid A.

(4) *Pyrogens.* Proceed as directed in §436.32(a) of this chapter, using a solution containing 5 milligrams of vancomycin per milliliter.

(5) *Moisture.* Proceed as directed in §436.201 of this chapter.

(6) pH. Proceed as directed in §436.202 of this chapter, using a solution containing 50 milligrams per milliliter.

(7) Heavy metals. Proceed as directed in §436.208 of this chapter.

(8) *Identity*. Proceed as directed in §436.211 of this chapter, using the 0.5 percent potassium bromide disc preparation as described in paragraph (b)(1) of that section.

[54 FR 20384, May 11, 1989; 54 FR 22838, May 28, 1989]

§ 455.285c Vancomycin hydrochloride injection.

(a) Requirements for certification—(1) Standards of identity, strength, quality, and purity. Vancomycin hydrochloride injection is a frozen, aqueous, iso-osmotic solution of vancomycin hydrochloride and a tonicity adjusting Each milliliter contains vancomycin hydrochloride equivalent to 5 milligrams of vancomycin. Its vancomycin content is satisfactory if it is not less than 90 percent and not more than 115 percent of the number of milligrams of vancomycin that it is represented to contain. It contains not less than 88 percent vancomycin factor B. It contains not more than 4 percent of any individual vancomycin related factor. It is sterile. It contains not

more than 0.33 U.S.P. Endotoxin Unit per milligram of vancomycin hydrochloride. Its pH is not less than 3.0 and not more than 5.0. The vancomycin used conforms to the standards prescribed by §455.86.

- (2) Labeling. It shall be labeled in accordance with the requirements of §432.5 of this chapter. In addition, this drug shall be labeled "vancomycin hydrochloride injection."
- (3) Requests for certification; samples. In addition to complying with the requirements of §431.1 of this chapter, each such request shall contain:
 - (i) Results of tests and assays on:
- (A) The vancomycin used in making the batch for vancomycin potency, chromatographic purity, moisture, heavy metals, and identity.
- (B) The batch for vancomycin content, chromatographic purity, sterility, bacterial endotoxins, pH, and identity.
- (ii) Samples, if required by the Director, Center for Drug Evaluation and Research:
- (A) The vancomycin used in making the batch: 10 packages, each containing approximately 300 milligrams.
 - (B) The batch:
- (1) For all tests except sterility: A minimum of 12 immediate containers.
- (2) For sterility testing: 20 immediate containers, collected at regular intervals throughout each filling operation.
- (b) Tests and methods of assay. Thaw the sample as directed in the labeling. The sample solution used for testing must be at room temperature.
- (1) Vancomycin content. Proceed as directed in §436.105 of this chapter, preparing the sample solution as follows: Using a suitable hypodermic needle and syringe, remove an accurately measured representative portion from each container immediately after thawing and reaching room temperature. Dilute with 0.1M potassium phosphate buffer, pH 4.5 (solution 4), to the reference concentration of 10 micrograms of vancomycin per milliliter (estimated).
- (2) Chromatographic purity. Proceed as directed in § 436.366 of this chapter. The relative amount of vancomycin B is not less than 88 percent and the relative amount of any related substance is not more than 4 percent.